L is, independently, phthalimido, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, hydrogen, halogen, hydroxyl, thiol, keto, carboxyl, NR^1R^2, $CONR^1$, amidine, guanidine, glutamyl, nitro, nitrate, nitrile, trifluoromethyl, trifluoromethoxy, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, azido, hydrazino, hydroxylamino, sulfoxide, sulfone, sulfide, disulfide, silyl, a nucleosidic base, an amino acid side chain, or a carbohydrate; and

each j and e is 0 or 1, with the sum of j and e equal to 1.

REMARKS

Claims 2-5, 7-12 and 33 are pending in the present application. Claim 33 has been amended herein. Because the amendments to claim 33 removes at least one issue for appeal (e.g., obviousness rejection), Applicant respectfully requests that they be entered into the record. See, M.P.E.P. §714.12.

I. No New Matter Has Been Added To The Claim

Claims 2-5, 7-12 and 33 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention. The Office Action mistakenly asserts that new matter was added to claim 33 upon deletion of the phrase "a single bond or." Applicant traverses the rejection and respectfully requests reconsideration thereof because the claims are amply supported by the specification.

In the response filed February 26, 2001, the particular relevant portion of claim 33 recited the following:

> each tether moiety T is [a single bond or] $-NH(R^1)NH-$, $-NH(R^1)O-$, $-NHR^2NH-$, $-NHR^2SO_2NH-$, $-NHR^1-$, $-N(R^4)_2$, -N=N-, O, S, Se, $-P(=O)(O)_2$, NH, OR^2, OR^3, malonato, pyrrolidinyl, piperidinyl, piperidinylmethylene, piperazinyl, or morpholino;

Significantly, no new matter rejection was proffered when claim 33 was introduced by the amendment of August 10, 2000. It was only upon deletion of "a single bond or" from claim 33 that the new matter rejection was proffered. The Office Action suggests several reasons for rejection, which upon careful inspection, are misplaced.

The Office Action asserts that the claims are directed to a mixture, not a single compound. Applicant agrees that claim 33 is directed to a mixture comprising a set of at least six compounds that have a common heterocyclic scaffold that bears functionalizable atoms, wherein the set of compounds is represented by one of the structures I, II, or III set forth in the claim. The Office Action then mistakenly asserts that it is not clear that Applicant had support for mixtures where "T is *not* a single bond." Applicant directs the Examiner's attention to, for example, the section titled "SUMMARY OF THE INVENTION" at page 2 of the specification wherein Applicant teaches:

> It is an object of the present invention to provide predictably diverse libraries of compounds based upon certain heterocyclic scaffolds functionalized with pluralities of chemical species. The chemical species may either be bonded directly to a functionalizable atom on the heterocyclic scaffold or may be so bonded through the intermediation of a tether moiety. It is preferred that the mixtures of the present invention comprise at least six chemical compounds.

Thus, Applicant's specification clearly supports chemical compounds wherein either: 1) the chemical species ("L" in claim 33) is bonded directly to the functionalizable atom on the heterocyclic scaffold (*i.e.*, T is a single bond), or 2) the chemical species is bonded to the functionalizable atom on the heterocyclic scaffold through the intermediation of a tether moiety (*i.e.*, T is a tether). As set forth above, Applicant also teaches that mixtures comprise at least six chemical compounds. In addition, the Examiner contradicts the very position proffered by admitting that "while these examples [libraries 59-62 and examples 109-113] show selections for T that are not single bonds..." Thus, Applicant clearly provides support in the specification for mixtures of chemical compounds where "T is *not* a single bond," thus complying with M.P.E.P. § 714.02.

The Office Action further mistakenly asserts that "removal of T as a selection in the Markush group is new matter" because there allegedly is no support for the "sub-generic" mixtures. First, Applicant has not removed "T" as a selection in the Markush group. Indeed, no "sub-generic mixtures" have been created upon removal of "a single bond or" nor does the Office Action identify any. Applicant has simply amended the claim by deleting one of the options for "T" (*i.e.*, deleting where "T" is a single bond). "T" remains recited in the claim and is followed by several members of a Markush group. Second, Applicant clearly has a right to claim that which he regards as his invention. Applicant clearly had possession of a mixture of chemical compounds where "T" is other than a single bond, as pointed out above where Applicant teaches that "T" can be a tether bonding the chemical species "L" to the functionalizable atom on the heterocyclic scaffold (see the section titled "SUMMARY OF THE INVENTION").

The Office Action admits that although libraries 59-62 and examples 109-113 "show selections for T that are not single bonds," but curiously purports that it is not clear support for removal of "or a single bond" from the claim. If the examples and libraries show that the compounds of the invention can have a tether (*i.e.*, T is not a single bond), then clearly they were in possession of a mixture of compounds that have tethers. The Office Action appears to further mistakenly suggest that because Applicant provides several examples in the specification of chemical compounds that do have T as a single bond, Applicant cannot cancel "or a single bond" without creating a "sub-genus." That Applicant provides examples of a particular embodiment of the invention, however, does not mandate that the particular element embodied remain claimed. There is no teaching in Applicant's specification that every mixture of chemical compound *must* have a compound where T is a single bond. Indeed, as pointed out above in the section titled "SUMMARY OF THE INVENTION," Applicant clearly taught chemical compounds that have a chemical species that is bonded to the functionalizable atom of the heterocyclic scaffold by either direct bonding, where T is a single bond, *or* by a tether. Applicant further teaches mixtures thereof. Thus, in some mixtures of six compounds, at least one of the compounds may comprise a tether, all of the compounds may comprise a tether, or none of the compounds may comprise a tether.

The Office Action concludes that in order for a negative limitation to be added to a claim, that particular limitation must be specifically recited in the specification. Although whether or not Applicant may actually agree, at least in part, with the conclusion drawn by the Examiner, the point is irrelevant because Applicant has not added a "negative limitation" to the claim, nor does the Examiner even identify one. Certainly, cancellation of a positively recited member of a Markush group does not create a "negative limitation."

In sum, Applicant was clearly in possession of a mixture of six chemical compounds, at the time of his invention, wherein "T" is not a single bond. Accordingly, Applicant requests that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

II. The Claimed Inventions Are Novel

Claims 2-5, 7-12 and 33 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Gordeev *et al.*, WO 96/33972, (hereinafter, the "Gordeev reference"). Applicant traverses the rejection because the Gordeev reference does not teach every element of the claimed invention.

The Office Action mistakenly asserts that the library compounds of Gordeev (directing Applicant to pages 34-35 and 81-85) have the claimed heterocyclic scaffold and substitution pattern. In particular, the Office Action asserts at page 5 that the Gordeev compounds have the same 2, 4, 6 substitution pattern on the pyrimidine ring. The structure on page 34 has an X moiety at the 5 position of the pyrimidine ring which is required to be other than H (X is defined at page 35, starting at line 5). Applicant's compounds do not read on these compounds. The compounds listed on page 81 of Gordeev have functional groups attached to the pyrimidine ring without tether moieties such as R_3 and R_4. The Examiner appears to suggest that, while admitting that the Gordeev compounds have R_3 and R_4 directly attached to the ring via bonds, because the third substituent is attached through a tether, the claim is anticipated. The Examiner is reminded that the standard for anticipation under § 102 is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224

U.S.P.Q. 409, 411 (Fed. Cir. 1984). Thus, as amended, the compounds of the present mixtures all recite that the tether moiety be other than a single bond and are not anticipated by the Gordeev reference. Accordingly, Applicant requests that the rejection under 35 U.S.C. § 102(a) be withdrawn.

III. The Claimed Inventions Are Not Obvious

Claims 2-5, 7-12 and 33 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,998,420 (hereinafter, the "Grandoni reference") in view of U.S. Patent No. 5,591,694 (hereinafter, the "Hamprecht reference") in further view of Gordon *et al.*, *J. Med. Chem.*, **1994**, *37*, 1385-1401 (hereinafter, the "Gordon reference"). Applicant traverses the rejection because, *inter alia*, the combination of references does not produce the claimed invention.

The Office Action mistakenly asserts that the sulfonylurea herbicides of Grandoni and Hamprecht read on compounds of the claimed mixtures. No selection of tether "T" and chemical substituent "L" of the claimed compounds, however, will give the thiourea compounds reported in the Grandoni and Hamprecht references. Further, the Gordon reference merely reports general aspects of combinatorial organic synthesis and does not, in any way, remedy the deficiencies of the Grandoni and Hamprecht references. The Office Action mistakenly asserts that compound "8 KIH-2031/DPX-PE 350" at page 6 of the Grandoni reference is within the scope of claim 33. "8 KIH-2031/DPX-PE 350," however, contains a $-CO_2Na$ substituent appended to the substituted carbocyclic moiety which, is not one of the substituents recited in claim 33. In regard to the disclosure of compound IIIa of the Hamprecht reference, Applicant has amended the claim by restructuring it to omit "halo" as a substituent when "L" is "substituted C_1-C_{10} alkyl." Applicant is not adding new matter to the claims but, rather, is simply amending the claims to delete positively recited elements and is, thus, claiming that which he regards as the invention. Thus, the combination of the cited references fails to produce any of the compounds recited in claim 33, as amended. Therefore, the combination of references fails to result in a *prima facie* case of obviousness. Accordingly, Applicant requests that the rejection under 35 U.S.C. § 103(a) be withdrawn.

IV. Conclusi n

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 564-8906 if there are any questions regarding Applicants' claimed invention. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

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Date: **July 19, 2001**

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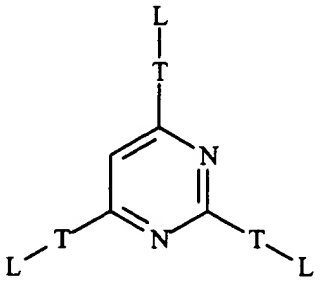
VERSION WITH MARKINGS TO SHOW CHANGES MADE

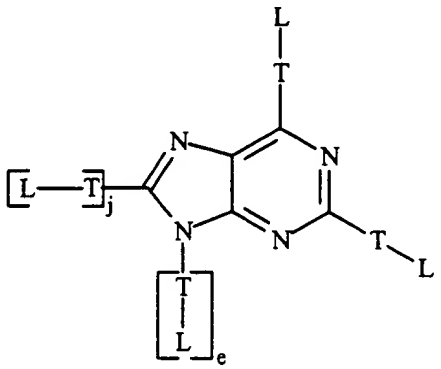
In the Claims:

Claim 33 has been amended as follows:

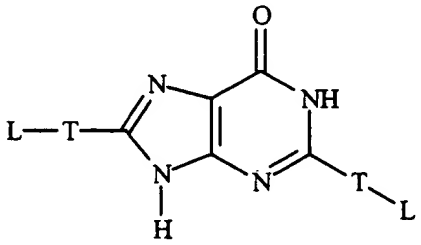
33. (Amended twice) A mixture comprising a set of at least six chemical compounds having a common heterocyclic scaffold bearing functionalizable atoms, wherein said set of compounds is represented by one of structures I, II or III:



I



II



III

wherein for structure I:

each tether moiety T is -NH(R^1)NH-, -NH(R^1)O-, -NHR^{2}NH-, -NHR^{2}SO$_2$NH-, -NHR^1-, -N(R^4)$_2$, -N=N-, O, S, Se, -P(=O)(O)$_2$, NH, OR^2, OR^3, malonato, pyrrolidinyl, piperidinyl, piperidinylmethylene, piperazinyl, or morpholino;

wherein R^1 is alkylene; R^2 is aryl; R^3 is H or C_1-C_{10} alkyl; R^4 is alkylenoxy; and

each chemical substituent L is, independently, C_1-C_{10} alkyl, [substituted C_1-C_{10} alkyl,] C_2-C_{10} alkenyl, substituted C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, substituted C_2-C_{10} alkynyl, C_4-C_7 carbocyclic alkyl, substituted C_4-C_7 carbocyclic alkyl, C_4-C_{10} alkenyl carbocyclic, substituted C_4-C_{10} alkenyl

carbocyclic, C_4-C_{10} alkynyl carbocyclic, substituted C_4-C_{10} alkynyl carbocyclic, a nitrogen, oxygen or sulfur containing saturated heterocycle, a substituted nitrogen, oxygen or sulfur containing saturated heterocycle, a benzo-fused heterocycle, a substituted benzo-fused heterocycle, a substituted or unsubstituted saturated mixed heterocycle; wherein each of the substituent groups is selected from a group consisting of alkyl, alkenyl, alkynyl, aryl, hydroxyl, alkoxy, benzyl, nitro, thiol, thioalkyl, thioalkoxy and halo; or

each chemical substituent L is, independently, substituted C_1-C_{10} alkyl, wherein each of the substituent groups is selected from a group consisting of alkyl, alkenyl, alkynyl, aryl, hydroxyl, alkoxy, benzyl, nitro, thiol, thioalkyl, and thioalkoxy; or

L is, independently, piperazine, pyridazine, pyrazine, triazine, phthalimido, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, hydrogen, halogen, hydroxyl, thiol, keto, carboxyl, NR^1R^2, $CONR^1$, amidine, guanidine, glutamyl, nitro, nitrate, nitrile, trifluoromethyl, trifluoromethoxy, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, azido, hydrazino, hydroxylamino, sulfoxide, sulfone, sulfide, disulfide, silyl, a nucleosidic base, an amino acid side chain, or a carbohydrate; and

wherein for structures II and III:

each tether moiety T is $-NH(R^1)NH-$, $-NH(R^1)O-$, $-NHR^2NH-$, $-NHR^2SO_2NH-$, $-NHR^1-$, $-N(R^4)_2$, -N=N-, O, S, Se, $-P(=O)(O)_2$, NH, OR^2, OR^3, malonato, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, imidazolyl, pyrrolyl, pyrazolyl, indolyl, 1H-indolyl, α-carbolinyl, carbazolyl, phenothiazinyl, phenoxazinyl, tetrazolyl, or triazolyl;

wherein R^1 is alkylene; R^2 is aryl; R^3 is H or C_1-C_{10} alkyl; R^4 is alkyleneoxy; and

each chemical substituent L is, independently, C_1-C_{10} alkyl, substituted C_1-C_{10} alkyl, C_2-C_{10} alkenyl, substituted C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, substituted C_2-C_{10} alkynyl, C_4-C_7 carbocyclic alkyl, substituted C_4-C_7 carbocyclic alkyl, C_4-C_{10} alkenyl carbocyclic, substituted C_4-C_{10} alkenyl carbocyclic, C_4-C_{10} alkynyl carbocyclic, substituted C_4-C_{10} alkynyl carbocyclic, C_6-C_{14} aryl, substituted C_6-C_{14} aryl, heteroaryl, substituted heteroaryl, a nitrogen, oxygen or sulfur containing heterocycle, a substituted nitrogen, oxygen or sulfur containing heterocycle, a mixed heterocycle,

or a substituted mixed heterocycle; wherein each of the substituent groups is selected from a group consisting of alkyl, alkenyl, alkynyl, aryl, hydroxyl, alkoxy, benzyl, nitro, thiol, thioalkyl, thioalkoxy and halo; or

L is, independently, phthalimido, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, hydrogen, halogen, hydroxyl, thiol, keto, carboxyl, NR^1R^2, $CONR^1$, amidine, guanidine, glutamyl, nitro, nitrate, nitrile, trifluoromethyl, trifluoromethoxy, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, azido, hydrazino, hydroxylamino, sulfoxide, sulfone, sulfide, disulfide, silyl, a nucleosidic base, an amino acid side chain, or a carbohydrate; and

each j and e is 0 or 1, with the sum of [J] j and e equal to 1.